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Comparison of 3D BOLD Functional MRI with Spiral Acquisition at 1.5 and 4.0 T

Yihong Yang,* Hen Wen,† Venkata S. Mattay,‡ Robert S. Balaban,† Joseph A. Frank,* and Jeff H. Duyn*

**Laboratory of Diagnostic Radiology Research, OIR, †Laboratory of Cardiac Energetics, NHLBI, and ‡Clinical Brain Disorders Branch, NIMH, National Institutes of Health, Bethesda, Maryland 20892*

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In order to investigate the merit of high field strength for BOLD-contrast-based functional magnetic resonance imaging (fMRI) studies, multishot gradient-echo fMRI experiments during motor cortex activation were performed on 1.5- and 4.0-T scanners with equivalent hardware, on the same volunteers. In these studies, artifactual vascular enhancement related to inflow effects was minimized, and large brain areas were covered by using a 3D scan technique. Temporal signal stability was optimized by using spiral readout gradients. The sensitivity for detection of activated regions was assessed by measuring the number of "activated voxels" and their average *t* score in predefined regions of interest. When comparing fMRI experiments with the same total scan time, performed on six subjects, and with acquisition parameters optimized for each field strength separately, the 4.0-T scanner proved to give superior results, with a 70% greater number of activated voxels and a 20% higher average *t* score for the activated voxels.

Key Words: **functional MRI; spiral scan; high field.**

INTRODUCTION

Functional imaging using gradient-echo MRI *allows* the study of brain activation, by dynamically measuring susceptibility changes related to the increase in the blood oxygen level upon activation (Ogawa *et al.*, 1990). The proposed mechanism for this signal increase is the reduced intravoxel phase dispersion of the magnetization due to decreases in the intravascular deoxyhemoglobin concentration. Some uncertainty remains about how this phase dispersion is generated and whether it originates primarily from the capillary bed or from larger vessels (Lai *et al.*, 1993).

At 1.5 T, the blood-oxygenation level-dependent (BOLD) signal changes in human brain are on the order of only a few percent and therefore difficult to reliably discern from fluctuations of the background signal caused by tissue motion and instrumental instabilities. Several researchers have observed a large (three- to fivefold) increase in BOLD signal changes in single-slice (2D) fMRI studies performed at 4.0 T (Turner *et al.*, 1993; Menon *et al.*, 1993; McKenzie *et al.*, 1993; Gati *et al.*, 1997). The increase in BOLD contrast could be a significant advantage in fMRI studies. It has been attributed to the increased susceptibility effects at higher fields, corresponding to an increase in the change of transverse relaxation rate ΔR_2^* in the capillary bed by a power of the field strength varying from 1 to 2 (Turner *et al.*, 1993; Gati *et al.*, 1997). Confounding factors in these studies are a lack of information regarding the level of the physiological background noise and effects of inflow (Duyn *et al.*, 1994). The ultimate benefit of high field strength for fMRI will be dependent on the contrast-to-noise ratio (CNR) and is likely to be much smaller than previously suggested. A preliminary study on field strength dependence of the fMRI signal, taking into account the background signal fluctuations related to scanner noise and physiologic fluctuations, has demonstrated a smaller (around 40%) improvement when the field strength is increased from 1.5 to 3.0 T (Bandettini *et al.*, 1994). The study used single-slice, single-shot EPI acquisition and compared CNR at various echo times.

The following study compares CNR values for fMRI experiments performed at 1.5 and 4.0 T, using multishot gradient-echo fMRI. Inflow effects are suppressed by performing 3D acquisitions (Duyn *et al.*, 1994), and spiral readout gradients are used to minimize instabilities related to physiologic fluctuations (Glover *et al.*, 1995; Yang *et al.*, 1996).

MATERIALS AND METHODS

Spiral Scanning

MR experiments were performed on 1.5- and 4.0-T GE scanners (General Electric, Milwaukee, WI), with identical maximum gradient strength (10 $mT \cdot m^{-1}$) and maximum slew rate (17 $T \cdot m^{-1} \cdot s^{-1}$). A standard clinical quadrature head coil was used at 1.5 T, and an

in-house-developed volume quadrature coil (Wen *et al.*, 1994) was used at 4.0 T. The estimated intrinsic signal-to-noise ratio (SNR) gain in human brain with the 4-T coil was 2.67 (=4/1.5), neglecting relaxation time differences (Singerman *et al.*, 1997). All studies were performed as part of an IRB-approved protocol at the National Institutes of Health.

A fast 3D gradient-echo technique with spiral acquisition (Yang *et al.*, 1996) was used in the studies. Spiral waveforms of 10-ms length (equivalent to duration of data acquisition window, TACQ) were applied on the x and y gradients. Six interleaves were collected to achieve a 3.8×3.8-mm^2 nominal in-plane resolution. Twenty-four phase encoding steps (with 96-mm FOV) were applied in the z direction, resulting in a 4-mm nominal resolution in the axial direction. In order to improve scan-to-scan signal stability, the zero-order gradient moments were kept constant across repetitions, and a quadratic radiofrequency (RF) phase modulation scheme was used with a periodicity of 8 (Yang *et al.*, 1996; Duyn, 1997).

Task Activation Studies

Functional MRI experiments with primary sensorimotor cortex stimulation were performed on six normal volunteers, at both 1.5- and 4.0-T scanners. Three data sets (with TE/TR = 12/24, 22/34, and 32/44 ms) were collected at 4.0 T, in order to find optimal sensitivity for detection of activated regions (defined as activation-related signal increase divided by standard deviation of the signal time course). TE was counted from the center of the RF pulse to the center of TACQ, which is a good indication of the "effective TE" for T_2^* effects in small activation clusters (Yang *et al.*, 1998). At 1.5 T, a TE/TR combination of 30/42 ms was used, which was close to optimum determined in a previous study (Yang *et al.*, 1996). The RF flip angle (FA) was set to the Ernst angle for gray matter in all cases.

In each functional activation study, time series of images were acquired with a constant total acquisition time of 4.8 min, during which the subject switched between rest and finger tapping every 20 s. In the 4.0-T studies, the numbers of scans acquired were 84, 60, and 46 for the TRs of 24, 34, and 44 ms, respectively, whereas the number of scans acquired at 1.5 T was 48. The stimulation protocol entailed self-paced (~2 Hz) finger tapping, involving sequential thumb-to-digit oppositions (in the order of 2, 3, 4, 5, 5, 4, 3, 2) with the dominant hand. The subjects were supplied with ear plugs due to the high levels of acoustic noise during scanning, and foam packs were applied to restrict head motion.

Data Processing

Data processing was performed offline on SunSPARC (Sun Microsystems, Mountain View, CA) and SGI-Indigo (Silicon Graphics, Mountain View, CA) workstations. On the 3D spiral data, an initial one-dimensional Fourier transform was performed in the phase-encode direction (longitudinal direction) after cosine apodization. Subsequently, a regridding algorithm with a Gaussian convolution window was used to resample the data on an orthogonal equidistant grid in the transverse plane (Yang *et al.*, 1996; Jackson *et al.*, 1991). Prior to Fourier transformations in the two axial directions, the data were apodized by a radial cosine filter starting at half-maximum radius. The actual image resolution was estimated from the functional data by computing the full width at half maximum of the spatial autocorrelation function (Friston *et al.*, 1994; Worsley and Friston, 1995; Xiong *et al.*, 1995) after image registration. The purpose of calculating the actual resolution in the functional data was to determine the degrees of freedom for the statistical evaluation, to allow a basis for comparison of the data at the two field strengths.

All images were registered using cubic spline interpolation in order to correct for rigid body motion between scans (Unser *et al.*, 1993; Thevenaz *et al.*, 1995). In order to evaluate the scan-to-scan stability, the standard deviation of the image intensity time course was calculated for each voxel in the brain and presented as a histogram. This measure of signal stability included effects of tissue motion and pulsation (such as are induced by cardiac and respiratory cycles), as well as scanner noise.

In order to establish the instrumental stability of the 1.5- and 4.0-T scanners, and to estimate its effect in the current study, time series data were also acquired on phantoms ($T_1 = 1500$ ms, $T_2 = 300$ ms). The time-course standard deviation was found to be below 0.35% at both field strengths, significantly lower than the physiologic noise levels at these fields (see below), and therefore not a determining factor in the evaluation of the relative sensitivity in the activation studies.

Statistical analysis of the functional data was performed by means of a Student t test in predefined region-of-interest (ROI), adjusted for total number of voxels in the ROI by a Bonferroni correction. For each subject, a ROI was defined covering the contralateral primary sensorimotor cortex, the premotor region, the parietal region, and the supplementary motor area. The total number of voxels in an ROI was typically 400, resulting in a Bonferroni-corrected significance threshold of $P < 6.25 \times 10^{-5}$ per voxel. The corresponding t cutoff was approximately 3.8 (one-sided probability of 0.025), and voxels with t score above the threshold were considered significantly activated. The total number of activated voxels and the average t score of the activated voxels in the ROI were calculated for each subject.

T_1 and T_2^* Measurements

In order to allow comparison of relaxation rates at 4.0 T with known values at 1.5 T, T_1 and T_2^* were measured at 4.0 T using gradient-echo spiral MRI sequences. For measurement of T_2^*, a series of images was acquired with varying TE (12, 22, 32, 42, 52 ms) and fixed TR (100 ms) and FA (20°). T_2^* maps were obtained by least-squares fitting of a single exponential decay to the data, on a voxel-by-voxel basis. For the determination of T_1 values, a series of images was acquired with varying TR (25, 50, 100, 250, 500, 1000, 2500, 5000 ms) and fixed TE (12 ms) and FA (45°). T_1 maps were obtained by least-squares fitting of a single exponential to the data, on a voxel-by-voxel basis.

RESULTS

Image Quality and Relaxation Times

Subsets of brain images acquired with the 3D spiral sequences at 1.5 and 4 T are shown in Fig. 1. The images at 4.0 T demonstrated a high signal intensity in central regions, attributed to the strong dielectric effects (Bomsdorf *et al.*, 1988; Barfuss *et al.*, 1990) at high field strengths. The effective in-plane resolution of the 4.0-T data was 1.68 pixel dimensions, which was about 20% larger than the 1.5-T data (1.40), as estimated from autocorrelation analysis. This phenomenon was attributed to the increased off-resonance related blurring (inherent to spiral imaging), as well as to T_2^* shortening, at higher field strengths.

The measured T_1 values in gray and white matter at 4.0 T are 1428 ± 168 and 945 ± 67 ms, respectively. The T_2^* values are 28.7 ± 4.3 and 42.6 ± 5.2 ms in the anterior and posterior gray matter, respectively, and 24.8 ± 3.5 and 36.6 ± 3.8 ms in the anterior and posterior white matter, respectively. These measured relaxation times are similar to previous results (Barfuss *et al.*, 1988; Kim *et al.*, 1994; Jezzard *et al.*, 1996) and a factor of about 2.5 times smaller than those found at 1.5 T.

Temporal Stability

Experimental noise values at 1.5 and 4.0 T, as determined by the standard deviation values of the image intensity time course in voxels across the brain, are summarized in Fig. 2. The figure shows composite histograms including all subjects. From the positions and shapes of the curves, information about the experimental noise can be derived. It appears that the noise in the 4.0-T data obtained at TE/TR = 12/24 ms is lower than the noise in the data obtained at TE/TR = 22/34 or 32/44 ms and the data obtained at 1.5 T (TE/TR = 30/42 ms). However, because of the fact that the distributions of the standard deviation are not equal across the various experimental conditions (as evidenced, e.g., by the varying extent of the tail), no easy quantitative assessment of the relative noise levels in the data can be made.

For completeness, an ROI-based temporal standard deviation value was calculated also for the primary sensorimotor cortex region. This resulted in similarly shaped histograms, with similar peak positions.

Overall Sensitivity

Results of the activation studies (number of activated voxels and their averaged *t* score) at 1.5 and 4.0 T are shown in Table 1. The largest activated area and highest *t* scores were observed in the studies at 4T with

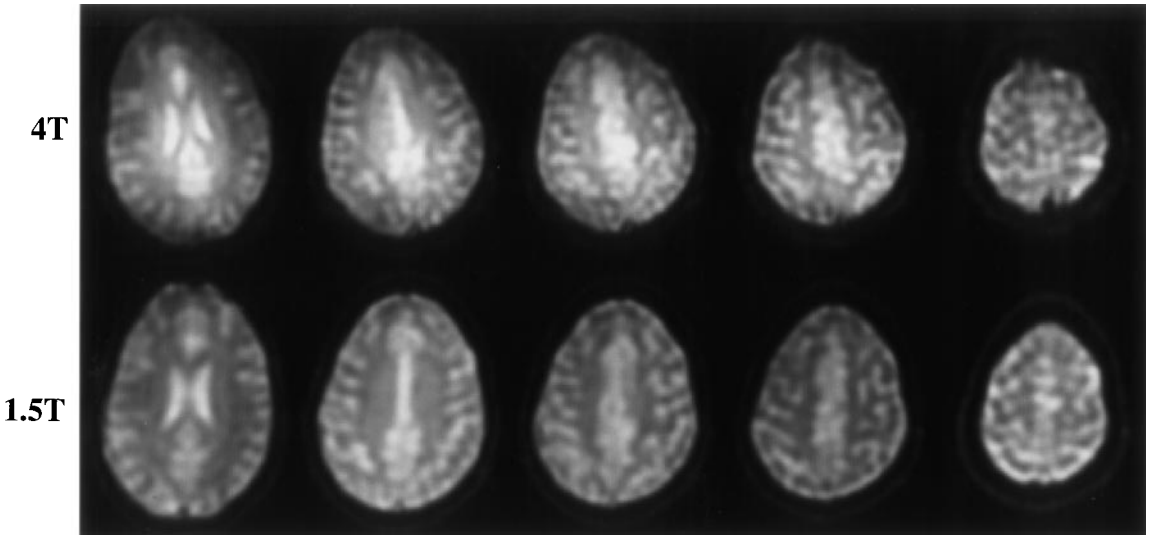

FIG. 1. Subsets of brain images acquired using 3D spiral fMRI at 1.5 T (TE/TR = 30/42 ms, FA = 5^0) and 4.0 T (TE/TR = 12/24 ms, FA = 5^0). The effective in-plane resolution was adjusted to 1.40 pixels for both image sets, by tuning the spatial apodization parameters.

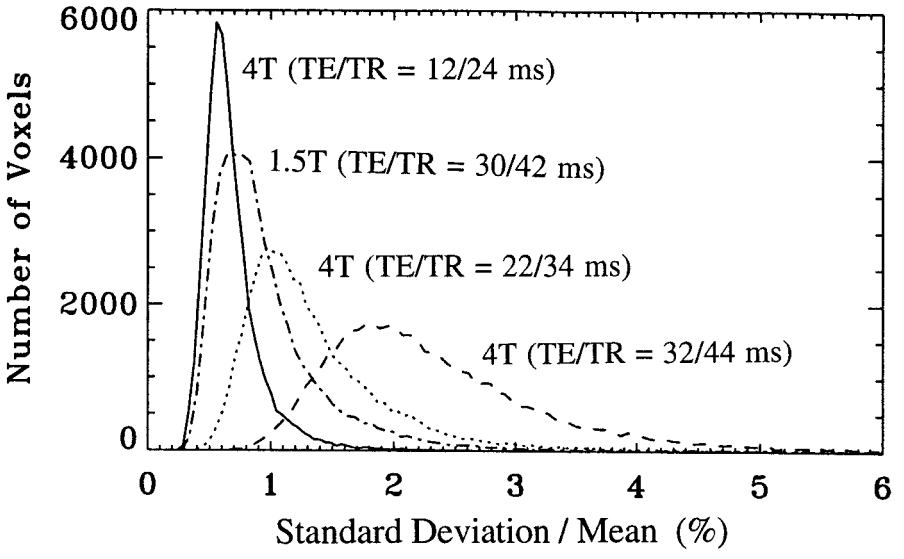

FIG. 2. Histograms of standard deviation of the image intensity time course including all voxels in the brain and all subjects. The four curves represent the studies at 1.5 T with TE/TR of 30/42 ms and the studies at 4.0 T with TE/TR settings of 12/24, 22/34, and 32/44 ms.

a TE/TR setting of 12/24 ms. This relatively low optimum value compared with earlier studies (Gati *et al.*, 1997; Bandettini *et al.*, 1994) is attributed to the improved temporal signal stability (reduced effect of physiologic fluctuations) and increased number of scans within the (fixed) study time. At this optimum setting, 70% more activated voxels and 20% higher average t scores were found at 4 T compared with the 1.5-T data. A paired Student t test showed that the number of activated voxels and average t score at 1.5 T are significantly lower than those at 4 T with TE/TR 12/24 ms ($P < 5 \times 10^{-3}$ and $P < 2 \times 10^{-3}$, respectively) and 22/34 ms ($P < 0.02$ and $P < 3 \times 10^{-3}$, respectively).

Figure 3 shows composite histograms of the ROI-based t score including all subjects for the studies at 4 and 1.5 T. Each curve represents both activated and nonactivated voxels within each ROI. The vertical line at $t = 3.8$ indicates the imposed separation between the activated and the nonactivated voxels. Comparison of the curves to the right of this cutoff suggests more activated voxels (area under the curve) and higher t score (center-of-mass of the curve) for the studies at 4 T with TE/TR settings of 12/24 and 22/34 ms than at 1.5 T.

Signal increases due to brain activation were calculated for the activated voxels within the ROIs. The signal changes (ΔS) were 1.35 ± 0.26% for the studies at 1.5 T (TE/TR = 30/42 ms) and 1.24 ± 0.25, 2.38 ± 0.38, and 3.52 ± 0.56% for the studies at 4 T with TE/TR settings of 12/24, 22/34, and 32/42 ms, respectively. The corresponding changes in ΔR_2^* were (assuming $\Delta R_2^* = \Delta S/\mathrm{TE}$ from Taylor series approximation) 0.45 s^{-1} at 1.5 T and 1.03, 1.08, and 1.10 s^{-1} for the three echo times at 4 T, respectively. One word of caution needs to be made at this point. The voxels contributing to the calculation of ΔS were selected using a fixed activation threshold of $t = 3.8$ and were not necessarily the same between 1.5 and 4.0 T. The calculated numbers should therefore be seen as indication of ΔS, and not necessarily hard values.

TABLE 1

Number of Activated Voxels (NAV) and Their Averaged t Score (ATS) in the Predefined ROIs at 4 and 1.5 T

	4 T			1.5 T
Volunteer	TE/TR = 12/24 (NAV/ATS)	TE/TR = 22/34 (NAV/ATS)	TE/TR = 32/44 (NAV/ATS)	TE/TR = 30/42 (NAV/ATS)
1	74/6.41	53/5.21	24/5.11	54/5.19
2	100/5.92	86/5.81	35/4.67	74/4.91
3	89/5.24	70/5.14	62/5.08	45/4.89
4	65/5.84	28/4.96	11/4.32	24/4.44
5	73/5.83	55/5.55	26/4.62	36/4.82
6	34/5.39	54/5.23	5/4.18	26/4.64
Mean	72.5/5.77	57.7/5.32	27.2/4.66	43.2/4.82
SD	22.7/0.42	19.4/0.31	20.2/0.38	18.9/0.26

Analysis at Similar Image Resolution

To allow comparison of the two field strengths at similar image resolutions, all data were reanalyzed with spatial apodization parameters adjusted for the 4.0-T data individually (less apodization), resulting in identical effective in-plane (x–y) resolutions of 1.40 pixel dimensions and identical through-plane (phase-encoding) resolutions of 1.2 pixels at both fields. The results of this analysis were very similar to the original results obtained with identical apodization param-

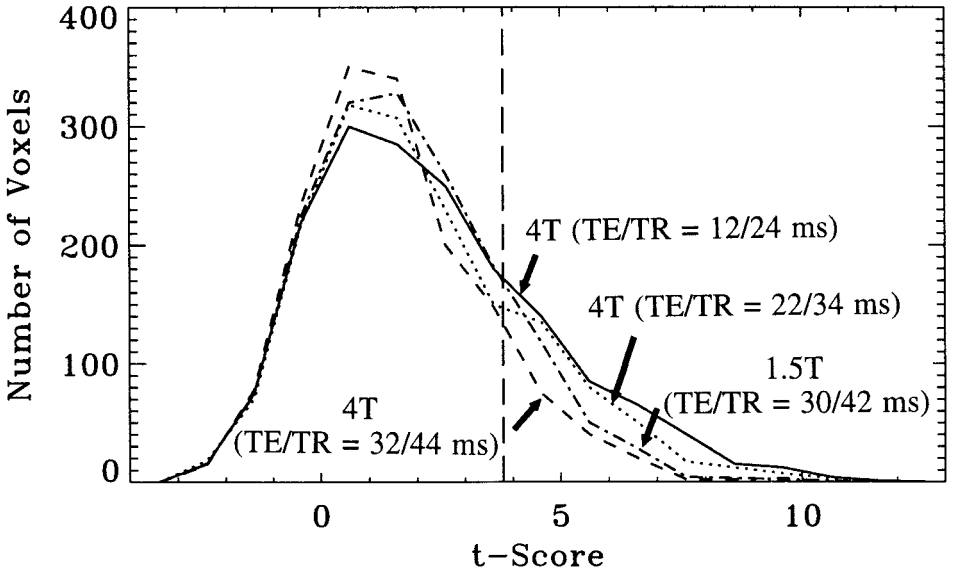

FIG. 3. Composite histograms of the ROI-based *t* score for the studies at 1.5 T with TE/TR of 30/42 ms and the studies at 4.0 T with TE/TR settings of 12/24, 22/34, and 32/44 ms. Voxels with a *t* score above 3.8 (cutoff indicated with a vertical line) were considered activated.

eters. Both the number of activated voxels and the average *t* score were within 5% of the original values.

DISCUSSION

The results presented above demonstrate certain benefits of high field scanners for functional MRI experiments based on BOLD contrast mechanisms, although, under the current conditions, the improvement in sensitivity appears smaller than suggested by earlier reports (Turner *et al.*, 1993; Menon *et al.*, 1993; McKenzie *et al.*, 1993; Gati *et al.*, 1997). In addition, the increase in ΔR_2^* with activation measured in the current high field study was somewhat smaller than earlier measurements (Turner *et al.*, 1993). The measured value of ΔR_2^* during activation motor cortex activation was about 2.4 times higher at 4.0 T than at 1.5 T. Given the effect–field relationship of $\Delta R_2^* = B_o^a$, this corresponds to a of around 1, somewhat below the earlier suggested range of $1 < a < 2$. On the other hand, under the conditions reported in this study, with voxel sizes of around $5 \times 5 \times 5$ mm, R_2^* was about the same factor (around 2.5) higher at 4.0 T. Therefore, when comparing fMRI experiments in which the functional effect (ΔS) is maximized (i.e., $\mathrm{TE} = T_2^* = 1/R_2^*$), in the first approximation no significant increase in percentage signal change with activation ($\Delta S/S$) is expected at higher magnetic field strengths. This is because $\Delta S/S = \mathrm{TE} \cdot \Delta R_2^* = \Delta R_2^*/R_2^*$, in which the increase in ΔR_2^* is counterbalanced by an increase in R_2^*. A gain in sensitivity at 4 T compared to 1.5 T is therefore to be expected primarily from the estimated SNR increase at 4 T, calculated at 1.9 (this includes effects of the increased T_1 at 4 T). However, when comparing average *t* scores in the activated regions (which takes into account the contribution of physiologic noise), with experimental settings optimized at each field strength individually, the improvement at 4 T is only 1.2. In addition, optimal results were not achieved at $\mathrm{TE} = T_2^*$, but at $\mathrm{TE} < T_2^*$. These observations suggest the presence of physiologic noise, which increases at higher fields (relative to intrinsic, i.e., electronic, noise), at least under the experimental conditions described in this study. Scanning at $\mathrm{TE} < T_2^*$ allows reduction of TR, which improves temporal resolution and potentially reduces the influence of physiologic fluctuations such as physiologic pulsations and subject motion (van Gelderen *et al.*, 1995). In addition, improved stability can also result from higher levels of CSF suppression at reduced TR.

Apart from B_o and TE, TR dependencies, the sensitivity of gradient-echo fMRI experiments is affected by background susceptibility effects, which are spatially varying. These susceptibility effects, which scale with B_o, lead to signal loss through intravoxel dephasing, as well as to blurring and/or image distortions. In order to avoid deterioration of fMRI image quality, both TE and TACQ could be reduced at higher field strength to scale with T_2^*. However, shortening TACQ would require an increase in the number of interleaves or a faster gradient slew rate. In the current study, identical hardware and acquisition methodology were used, and the increased blurring at 4.0 T was equilibrated by stronger apodization of the 1.5-T data. Alternatively, the increased blurring at 4.0 T could be alleviated by postprocessing using separately recorded field (B_o) maps or by shortening the TACQ.

In summary, 3D functional MRI experiments with spiral acquisition showed 70% more activated voxels

and 20% higher average *t* scores for the activated voxels at 4.0 T than at 1.5 T, using identical gradient hardware. For the same effective image resolution, higher field strengths require shorter acquisition windows, leading to higher gradient hardware demands, or an increased number of interleaves (pulse sequence repetitions).

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